LETTER TO THE EDITOR



Can the host immune response against SARS-CoV2 also cause an anticancer effect?

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Abstract

During the COVID-19 pandemic, it is important to assure the safety and management of cancer patients. Despite preliminary studies revealed that patients with cancer are more susceptible to infection and have poorer prognosis than other infected patients without cancer, mortality from COVID-19 in cancer patients appears to be principally driven by age, gender, and comorbidities. So, we have some comments about the pathogenesis attributed to the COVID-19 disease and cancer relationship and determination of subgroups in this and oncoming studies. Variable effects of anticancer treatments on the patient's immune system are yet to be elucidated. On the other hand, the effect of SARS-CoV-2 virus on tumor microenvironment or immune responses in cancer is not yet fully proven. Very recently, Challenor and her colleague reported a case with classical Hodgkin lymphoma with stage IIIs disease, which went into remission without corticosteroid or immunochemotherapy. They assumed that the putative mechanisms of action include cross-reactivity of pathogen-specific T cells with tumor antigens and natural killer cell activation by inflammatory cytokines produced in response to infection. During the course of COVID-19 disease, immune checkpoint blockade effect might be induced naturally.

Keywords COVID-19 disease · Tumor immune responses · Tumor microenvironment · Immune checkpoint blockage effect

To the Editor

During the COVID-19 pandemic, it is important to assure the safety and management of cancer patients. Preliminary studies revealed that patients with cancer are more susceptible to infection and have poorer prognosis (more severe or critical symptoms, higher rates of intensive care unit admission or death) than other infected patients without cancer [1–3]. It has been attributed to their systemic immune suppressive state caused by the malignancy, anticancer treatment and surgery. Additionally, patients with cancer receiving systemic anticancer treatments have been postulated to be at a higher risk from the disease than their counterparts who are not receiving anticancer treatment. However, provided by these studies mostly retrospective and including limited number of patients, any results need to be interpreted vigilantly and criticized. In a current prospective, largest

First of all, it is well established that COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) ultimately can become a lethal disease of hyperinflammation and respiratory dysfunction [5]. Acute respiratory distress syndrome (ARDS) is the main cause of death induced by the cytokine storm in COVID-19 disease [6]. Also, rapid multiple organ dysfunction syndrome (MODS) which is multifactorial process and especially proposed mechanisms for MODS includes a hypercoagulable state with micro- and macro-circulatory thrombosis and eventually fibrosis [7]. Significant increase in serum D-dimer levels

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cohort study to date belongs to Lee colleagues including 800 patients with a diagnosis of cancer and symptomatic COVID-19, it has been reported that after adjusting for age, gender, and comorbidities, chemotherapy in the past 4 weeks had no significant effect on mortality from COVID-19 disease, when compared with patients with cancer who had not received recent chemotherapy. [4]. Also, they concluded that mortality from COVID-19 in cancer patients appears to be principally driven by age, gender, and comorbidities. So, we have some comments about the pathogenesis attributed to the COVID-19 disease and cancer relationship and determination of subgroups in this and oncoming studies.

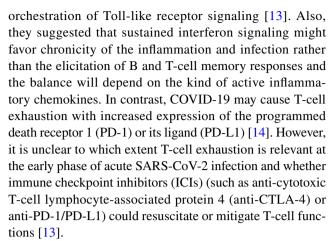
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(above 1 µg/mL) has been shown to be a strong risk factor for death in these patients [8]. Anti-inflammatory and maybe anti-viral properties of heparin may have additional benefit in these patients [9]. At present, there are no Food and Drug Administration (FDA)-approved drugs specifically indicated for the treatment of COVID-19 disease, with the exception of remdesivir (the FDA granted remdesivir an Emergency Use Authorization for the treatment of hospitalized patients with severe COVID-19). Treatment of COVID-19 cytokine storm is primarily consists of supportive treatment of respiratory dysfunction with high-flow oxygen, corticosteroids, heparin, therapeutic plasma exchange and mechanical ventilation for fulminant disease. Variable effects of anticancer treatments on the patient's immune system are yet to be elucidated. As known, cancer is accompanied by immunomodulatory cytokines, decreased proinflammatory danger signals, impaired immune cell functions which is conflicting with the state that severe COVID-19 patients faced [10]. Immunosuppressive effect of the anti-neoplastic agents or corticosteroids may represent the factor improving prognosis in the active anticancer therapy receiving group of patients. In addition to this, heparin which we frequently use for prophylactic as well as for therapeutic purposes in cancer patients may have provided mild COVID-19 disease course especially after the viremic phase.

On the other hand, the effect of SARS-CoV-2 virus on tumor microenvironment or immune responses in cancer is not yet fully proven. Very recently Challenor and her colleague reported that a patient with Epstein-Barr virus (EBV)-positive classical Hodgkin lymphoma with stage IIIS disease was admitted with breathlessness and wheeze and was diagnosed with PCR-positive SARS-CoV-2 pneumonia shortly after diagnosis [11]. It has been pointed out that after 11 days of best supportive ward-based care for COVID-19, the patient was discharged to convalence at home. Four months later, palpable lymphadenopathy reduced and an interim PET/CT scan revealed widespread resolution of the lymphadenopathy and reduced metabolic uptake throughout without corticosteroid or immune-chemotherapy. They hypothesized that the SARS-CoV-2 infection triggered an anti-tumor immune response, as had been described with other infections in the context of high-grade non-Hodgkin lymphoma [12]. They assumed that the putative mechanisms of action include cross-reactivity of pathogen-specific T cells with tumor antigens and natural killer cell activation by inflammatory cytokines produced in response to infection.

Melenotte et al. tried to describe the putative immune scenarios associated with protective immune responses during COVID-19 infection. The efficient priming of effector type 1 CD8+cytotoxic T cells, CD4+T helper cells for B cell maturation leading to the resolution of COVID-19 by the eradication of virally infected cells and acceleration of lung tissue repair may be provided through the appropriate



As we know, in cancer treatment, ICIs are used due to their role of blocking checkpoint proteins from binding with their partner proteins and consequently allowing the T cells to kill cancer cells. Monoclonal antibodies against CTLA-4 or PD-1 or PD-L1 reverse the exhaustion of cytotoxic T lymphocytes thus leading to the elimination of tumor cells via the re-induction of the "natural" function of the T-cell population [15]. As mentioned above, these diseases in which adaptive immune cells plays the leading role might be alleviated by the immune responses provided by the infections. During the course of COVID-19 disease, this immune checkpoint blockage effect might be induced naturally. Specifically, we believe that cancer patients whom tumor have the potential to get benefit from checkpoint inhibition and also recovered from COVID-19 disease should be the subject of research. Additionally, epigenomic and genomic studies might be conducted to elucidate the immunopathology.

In summary, we think that better designed research is needed to clarify the outcome of cancer patients who overcome COVID-19 disease and the shape of the immune system in the presence of both.

Declarations

Conflict of interest The authors indicated no potential conflicts of interest

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